AMENDMENT

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Previously presented): Edible plant material comprising transgenic plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible plant material exhibits an increased concentration of resveratrol glucoside as compared to edible plant material consisting of non-transgenic plant cells of the same cell type grown under the same conditions.

2. (Previously presented): The edible plant material of Claim 1, wherein said edible plant material is suitable for consumption as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical in the form of a live or harvested whole plant or plant part.

3. (Previously presented): The edible plant material of Claim 1, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.

4. (Previously presented): The edible plant material of Claim 2, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.

5. (Previously presented): The edible plant material of Claim 1, 2, 3 or 4, wherein said plant is a legume.

6. (Previously presented): The edible plant material of Claim 5, wherein said plant is alfalfa.

7. (Previously presented): The edible plant material of Claim 5, wherein said plant is soybean.

8. (Previously presented): A composition comprising edible plant material, said edible plant material comprising transgenic plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein the percentage of resveratrol glucoside in said composition obtained by adding a given weight of said edible plant material comprising said transgenic plant cells to said composition is higher than the percentage of resveratrol glucoside obtainable by adding instead the same weight of edible plant material consisting of non-transgenic plant cells of the same cell type grown under the same conditions to said composition.

9. (Previously presented): The composition of Claim 8, wherein said composition is suitable for consumption as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical.

10. (Previously presented): The composition of Claim 8, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.

11. (Previously presented): The composition of Claim 9, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.

12. (Previously presented): The composition of Claim 8, 9, 10 or 11, wherein said plant is a legume.

13. (Previously presented): The composition of Claim 12, wherein said plant is alfalfa.

14. (Previously presented): The composition of Claim 12, wherein said plant is soybean.

15. (Previously presented): An edible plant comprising transgenic plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible plant exhibits an increased concentration of resveratrol glucoside as compared to an edible plant comprising non-transgenic plant cells of the same cell type grown under the same conditions.

16. (Previously presented): The edible plant of Claim 15, wherein said edible plant is suitable for consumption as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical in the form of a live or harvested whole plant or a plant part.

17. (Previously presented): The edible plant of Claim 15, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.

18. (Previously presented): The edible plant of Claim 16, wherein said resveratrol synthase transgene encodes the amino acid sequence of SEQ ID NO:2.

19-20. (Canceled)

21. (Previously presented): The edible plant of Claim 15, 16, 17, or 18, wherein said plant is a legume.

22. (Previously presented): The edible plant of Claim 21, wherein said plant is alfalfa.

23. (Previously presented): The edible plant of Claim 21, wherein said plant is soybean.

24. (Previously presented): Seed from the edible plant of Claim 15, 16, 17 or 18.

25. (Previously presented): Progeny from the edible plant of Claim 15, 16, 17 or 18.

26. (Previously presented): Progeny from the seed of Claim 24.

27. (Currently amended): A method of improving the nutritional value of an edible plant comprising:

transforming cells from said plant with a DNA construct comprising at least one open reading frame encoding for resveratrol synthase under expression control of a constitutive promoter to form transgenic plant cells; and

cultivating said transgenic plant cell ~~under conditions conducive to regeneration and plant growth and under conditions conducive to the~~ to allow accumulation of p-coumaryl CoA and malonyl CoA precursors and ~~to minimizing~~ minimization of the concentration of β-glucosidases active on resveratrol glucoside,

wherein said edible plant exhibits an increased concentration of resveratrol glucoside as compared to an edible plant comprising non-transgenic plant cells of the same cell type grown under the same conditions.

28. (Previously presented): The method of Claim 27, wherein said open reading frame encodes the amino acid sequence of SEQ ID NO:2.

29. (Previously presented): A method of using an edible plant comprising

transforming plant cells of said edible plant with a resveratrol synthase transgene under the control of a constitutive promoter to form transgenic plant cells whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible plant exhibits an increased concentration of resveratrol glucoside as compared to an edible plant comprising non-transgenic plant cells of the same cell type grown under the same conditions and

consuming said edible plant to provide a nutraceutical benefit to a human or animal.

30. (Previously presented): The method of Claim 29, wherein said open reading frame encodes the amino acid sequence of SEQ ID NO:2.

31. (Withdrawn): A method of producing isolated resveratrol glucoside comprising

transforming a non-transgenic plant cell with a DNA construct comprising at least one open reading frame encoding for resveratrol synthase under expression control of a constitutive promoter to form said transgenic plant cell; and

cultivating said transgenic plant cell under conditions conducive to regeneration and plant growth and under conditions conducive to the accumulation of p-coumaryl CoA and malonyl CoA precursors and the suppression of β-glucosidases, wherein said transgenic plant cell exhibits an increased concentration of resveratrol glucoside as compared to non-transgenic plant cells of the same cell type grown under the same conditions; and

isolating said resveratrol glucoside from said transgenic plant cell.

32. (Withdrawn): The method of Claim 31, wherein said open reading frame is SEQ ID NO:2.

33. (Withdrawn): The method of Claim 31 or 32, wherein said isolated resveratrol glucoside is suitable for consumption as a nutritional supplement, an animal feed supplement, or a nutraceutical.

34. (Currently amended): A method for producing a transgenic plant cell having increased resveratrol glucoside concentration comprising

transforming a non-transgenic plant cell with a DNA construct comprising at least one open reading frame encoding for resveratrol synthase under expression control of a constitutive promoter to form said transgenic plant cell; and

cultivating said transgenic plant cell ~~under conditions conducive to regeneration and plant growth and under conditions conducive to the~~ to allow accumulation of p-coumaryl CoA and malonyl CoA precursors and ~~to minimizing~~ minimization of the concentration of β-glucosidases active on resveratrol glucoside,

wherein said transgenic plant cell exhibits an increased concentration of resveratrol glucoside as compared to non-transgenic plant cells of the same cell type grown under the same conditions.

35. (Previously presented): The method of Claim 34, wherein said open reading frame encodes the amino acid sequence of SEQ ID NO:2.

36. (Previously presented): The method of Claim 34 or 35, wherein said plant is a legume.

37. (Previously presented): The method of Claim 36, wherein said plant it alfalfa.

38. (Previously presented): The method of Claim 36, wherein said plant is soybean.

39. (Previously presented): A method of increasing disease resistance in an edible plant comprising transforming cells of said plant with a resveratrol synthase transgene under the control of a constitutive promoter whereby said transgenic plant cells accumulate resveratrol glucoside upon expression of said resveratrol synthase transgene, wherein said edible plant exhibits an increased concentration of resveratrol glucoside as compared to an edible plant comprising non-transgenic plant cells of the same cell type grown under the same conditions.

40. (Previously presented): The method of Claim 39, wherein said open reading frame encodes the amino acid sequence of SEQ ID NO:2.

41. (Currently amended): A method for decreasing spoilage of an edible plant or plant parts after harvesting comprising

before harvesting, transforming cells from said plant with a DNA construct comprising at least one open reading frame encoding for resveratrol synthase under expression control of a constitutive promoter to form transgenic plant cells; and

cultivating said transgenic plant cell ~~under conditions conducive to regeneration and plant growth and under conditions conducive to~~ to allow the accumulation of p-coumaryl CoA and malonyl CoA precursors and ~~to minimizing~~ minimization of the concentration of β-glucosidases active on resveratrol glucoside, wherein resveratrol glucoside accumulates in said transgenic plant cells,

whereupon harvesting, said plant exhibits an increased concentration of resveratrol glucoside as compared to a plant comprising non-transgenic plant cells of the same cell type grown under the same conditions.

42. (Previously presented): The method of Claim 41, wherein said open reading frame encodes the amino acid sequence of SEQ ID NO:2.

43-57. (Canceled)

58. (Previously presented): Seed from the edible plant of Claim 21.

59. (Previously presented): Seed from the edible plant of Claim 22.

60. (Previously presented): Seed from the edible plant of Claim 23.

61. (Previously presented): Progeny from the edible plant of Claim 21.

62. (Previously presented): Progeny from the edible plant of Claim 22.

63. (Previously presented): Progeny from the edible plant of Claim 23.

64. (Previously presented): Progeny from the seed of Claim 21.

65. (Previously presented): Progeny from the seed of Claim 22.

66. (Previously presented): Progeny from the seed of Claim 23.

67. (Previously presented): The edible plant of Claim 15, wherein said edible plant is useful as a source for isolated resveratrol glucoside.

RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 1-18, 21-42, and 58-67 are pending. Claims 31-33 have been withdrawn from consideration. No claims were allowed in the Action. Applicants have amended claims 27, 34, and 41. These amendments were made to clarify the language of the claims. They do not add any additional limitations to the claims.

B. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claims 27, 28, 34-38, 41, and 42 under 35 U.S.C. §112, second paragraph. The Action asserts that the phrase "under conditions conducive to the accumulation of..." in claims 27, 34, and 41 is indefinite because the metes and bounds of the limitation are unclear. In addition, the Action contends that the phrase "to minimizing the concentration of β-glucosidase active on resveratrol glucoside" is in an improper grammatical form and is indefinite because the metes and bounds of this limitation are unclear. Applicants traverse this rejection.

Claims 27, 34, and 41 have been amended to recite "cultivating said transgenic plant cell to allow the accumulation of p-coumaryl CoA and malonyl CoA precursors and minimization of the concentration of β-glucosidases active on resveratrol glucoside..." This language is fully definite under § 112, second paragraph. The Specification teaches that the accumulation of resveratrol glucoside is favored in plant tissues which contain the necessary biosynthetic precursors (p-coumaryl CoA and malonyl CoA) and low levels of β-glucosidases (Specification, p. 18, lines 10-12). Such conditions are most likely to be present in non-stressed tissues, rather than wounded or infected tissues (Specification, p. 18, lines 12-14). This is in contrast to earlier publications describing resveratrol synthase sequences under the control of its native promoter,

which required fungal infection or similar stresses to induce the synthesis of resveratrol synthase (see Specification, p. 3, lines 4-25).

A proper evaluation of the claims under § 112, second paragraph, requires that the claims be read in light of the specification as interpreted by one of ordinary skill in the art. Based on the teachings of the specification, those of ordinary skill in the art would understand that cultivating transgenic plant cells of the invention under normal growth conditions allows the accumulation of p-coumaryl CoA and malonyl CoA precursors and minimization of the concentration of β-glucosidases active on resveratrol glucoside, as recited in the claims.

Furthermore, Applicants refer to the references submitted with their previous response filed November 24, 2003, as additional evidence of the common knowledge of those of ordinary skill in the art. For example, Applicants provided references teaching that: ACC carboxylase catalyzes the production of malonyl CoA in plants, and increased activity of ACC is well known in the art to be associated with optimal lighting (Hunter *et al.*, 1998); the synthesis of p-coumaryl CoA from phenylalanine requires three enzymes, and that the activity of these enzymes is stimulated by light (Hahlbrock *et al.*, 1970; Bell-Lelong *et al.*, 1997; and Kubasek *et al.*, 1992); that *β*-glucosidases are stored in cells or compartments separated from glucosides, and when the cells are crushed or stressed (such as by fungal infection, UV damage, or wounding), the *β*-glucosidases are released and can then act on their substrates (Cicek *et al.*, 1998; White *et al.*, 1998; Poulton *et al.*, 1994).

In view of the above, Applicants submit that the claims are definite in light of the specification as interpreted by one of ordinary skill in the art. Withdrawal of the rejection is respectfully requested.

C. **Rejection of Claims Under 35 U.S.C. §102(a)**

The Action rejected claims 1, 2, 15, 16, 24-27, 29, 34, 39, 41, and 67 under 35 U.S.C. §102(a) as being anticipated by Leekband and Lorz (1998). The Action states that Leekband and Lorz disclose edible plant material, specifically barley and wheat, comprising transgenic plant cells transformed with a resveratrol synthase transgene under the control of a constitutive promoter, and a method of making said edible plant material. Applicants traverse this rejection.

Leekband and Lorz do not teach a resveratrol synthase transgene under the control of a ***constitutive*** promoter. Rather, the resveratrol synthase transgene disclosed by Leekband and Lorz was under the control of an ***inducible*** promoter. Specifically, plasmid pGBI contained the *Vst1* gene under the control of the homologous Vst1 promoter with enhancer sequences from CaMV, and plasmid pGBII contained the *Vst1* gene under the control of the ***homologous Vst1 promoter*** without enhancer sequences (see page 1005, column 2; and FIGs. 1C and 1D). Studies demonstrating the induction of the Vst1 promoter and expression of the *Vst1* gene are described on page 1008, column 1 to page 1009 column 1. Furthermore, the enhancer sequences had no influence on promoter induction and only worked as transcription-activating elements (see page 1011, column 1). All elements in the claims have therefore not been shown in the cited reference and thus the claims cannot be anticipated.

In view of the foregoing, removal of the rejection is respectfully requested.

D. **Rejection of Claims Under 35 U.S.C. § 103**

Claims 1-18, 21-42, and 58-67 stand rejected under § 103(a) as unpatentable over Schroder in view of Comai, and further in view of Tropf, Leekband and Lorz, and Applicants' admission.

The Action alleges that it would have been obvious to modify the resveratrol synthase transgene of Schroder with the promoter of Comai to constitutively express a resveratrol transgene in a transgenic plant. Further, the Action argues that Tropf teaches a transgene encoding the amino acid sequence of SEQ ID NO:2, and that Applicants admitted that the transgene taught by Tropf encodes the amino acid sequence of SEQ ID NO: 2. The Action also states that Leekband and Lorz teach that it was obvious to operably link a constitutive promoter to a resveratrol synthase gene and transform a plant. Applicants traverse this rejection.

There is no motivation or suggestion to combine the resveratrol transgene taught by Schroder with the promoter taught by Comai. It is recognized in the Action that Schroder does not specifically teach that the resveratrol gene can be operably linked to a constitutive promoter. It is also recognized in the Action that Comai does not teach operably linking the CaMV 35s enhanced MAS promoter with a resveratrol synthase gene. The Action nonetheless argues that one of ordinary skill in the art would have been motivated to combine these references. However, the Action failed to identify where Schroder or Comai even suggest the desirability of constitutively expressing the resveratrol synthase gene in a plant, let alone the functionality of the combination.

The motivation to combine references must be found in the cited prior art or in the knowledge generally available to one of skill in the art, not in Applicants' specification. *See In re Vaeck*, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991), *see also*, M.P.E.P. § 2142. Here, it appears that the Action, without instruction from the prior art, assumed that the skilled artisan would follow the same inventive path as Applicants. However, the Action cannot piece together the prior art based on the teaching of Applicants to arrive at the hindsight conclusion that the claimed invention is obvious. *In re Carroll*, 202 USPQ 571 (CCPA 1979).

The prior Action cited column 2, lines 30-35 and column 4, lines 19-31 of Schroder as suggesting the use of other promoter sequences operably linked to the resveratrol synthase gene (see sentence bridging pages 6 and 7 of the Action dated January 14, 2003). However, these passages are vague and fail to provide the requisite motivation. For example, the passage at column 2, lines 30-35 reads in relevant part "DNA sections [of the stilbene synthase gene] may be replaced by other DNA sections which act in essentially the same way." The motivation to combine is not supported on the record by fact.

The Action has also failed to identify in the cited art a basis for concluding that one of skill in the art would have a reasonable expectation that a resveratrol synthase transgene could be successfully expressed in a plant from a constitutive promoter to accumulate resveratrol glucoside. First, Schroder has not been shown to teach a resveratrol synthase gene with anything other from its homologous promoter. Given the complexity of successfully introducing and expressing a given coding sequence, particularly with heterologous combinations of expression elements not found in nature, an expectation of success in expressing a resveratrol synthase gene from a heterologous constitutive promoter would have been absent but for the teaching of Applicants' disclosure.

A basis has also not been presented in the cited art for concluding that one of skill in the art would have a reasonable expectation that transgenic plant cells would accumulate resveratrol glucoside upon expression of the constitutively expressed resveratrol synthase transgene. The resveratrol synthase gene produces resveratrol, not resveratrol glucoside. The conversion of resveratrol to resveratrol glucoside is catalyzed by a glucosyl transferase. One of ordinary skill in the art would not reasonably expect that a plant that does not naturally produce resveratrol would

possess an endogenous glucosyl transferase capable of acting upon resveratrol to produce resveratrol glucoside.

To establish a *prima facie* case of obviousness, there must be a reasonable expectation of success. The present rejection appears to rely on an "obvious to try" rationale, which is prohibited by the Federal Circuit.

Furthermore, Applicants' claimed invention provided unexpected results that are of a significant, practical advantage. A greater than expected result is a factor pertinent to the legal conclusion of obviousness. MPEP § 716.02(a). Even if it is assumed for purposes of argument that Schroder and Comai are properly combined, which they are not, they would at best have led one to predict the production of free resveratrol. Applicants' invention, however, provided the unexpected result of resveratrol glucoside accumulation in a somewhat tissue specific manner. This unexpected accumulation of resveratrol glucoside in plants provides significant, practical advantages. For example, as described in the specification, resveratrol glucoside has been reported to have health benefits (see *e.g.*, page 5, lines 3-19). Thus, the increased concentration of resveratrol glucoside in the transgenic plant cells would be advantageous as, for example, a nutritional supplement or nutraceutical.

For the reasons described above, the present invention is patentable over Schroder in view of Comai at least because: (1) there was no motivation or suggestion to combine the references; (2) there was no reasonable expectation of success; and (3) the present invention provided unexpected results.

Furthermore, that Tropf discloses the amino acid sequence of SEQ ID NO: 2 does not overcome any of the above-mentioned deficiencies in Schroder and Comai; and, as discussed in

regard to the § 102(a) rejection, Leekband and Lorz have not been shown to teach or suggest a constitutive promoter as alleged in the Action.

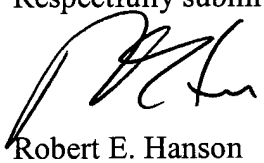
In view of the foregoing, Applicants respectfully request the removal of the rejection under 35 U.S.C. § 103.

E. Conclusion

This is submitted to be a complete response to the referenced Office Action. In conclusion, Applicant submits that, in light of the foregoing remarks, the present case is in condition for allowance and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned at (512) 536-3085 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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